REMARKS

Claims 1-18 and 33-53 are pending in this application. Claims 1, 8, 33, and 43 have been amended. Support for the amendments appears in, e.g., page 5, lines 14-21, and page 7, lines 19-20. No new matter is added.

Applicants request return of an initialed Form 1449 for the a Supplemental Information Disclosure Statement submitted for this case on December 11, 2003 in the next communication from the Examiner.

Rejection under 35 U.S.C §102(b)

Claims 1-7 and 50 are rejected as anticipated by Liversidge et al., U.S. Pat. No. 5,145,684 ("Liversidge"). The rejection is traversed to the extent it is applied to the claims as amended.

Claim 1, from which depends claims 2-7, has been amended so that it is drawn to a hydrophilic inclusion complex that consists essentially of nano-sized particles of a water-insoluble lipophilic compound surrounded by and entrapped within an amphiphilic polymer.

Liversidge does not describe an inclusion complex that is required by the claims. An inclusion complex is understood in the art as (definition taken from IUPAC Compendium of Chemical Terminology, 2nd Ed., 1997):

> **inclusion compound (inclusion complex)**
> A complex in which one component (the host) forms a cavity, or, in the case of a crystal, a crystal lattice containing spaces in the shape of a long tunnel or channels in which molecular entities of a second chemical species (the *guest*) are located. There is no covalent bonding between guest and host, the attraction being generally due to *van der Waals forces*. If the spaces in the host lattice are enclosed on all sides so that the test species is 'trapped' as in a cage, such compounds are known as *clathrates* or 'cage' compounds'.

Liversidge does not describe a particle that exists as an inclusion complex. To the contrary, it describes "dispersible particles consisting essentially of a crystalline drug substance having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less than about 400 nm". (Abstract).

Claim 1 also requires that the lipophilic compound is surrounded by and entrapped within the polymer. Liversidge also fails to describe this feature of the claimed invention. It teaches instead (col. 4, l. 28-33):

> [The] particles contain a discrete phase of a drug substance...having a surface modifier adsorbed on the surface thereof. Useful surface modifiers are ... those which physically adhere to the surface of the drug substance...

For the foregoing reasons, Liversidge fails to describe all the features of claim 1, from which the remaining claims subject to the rejection depend. Reconsideration and withdrawal of the rejection for anticipation is requested.

Rejection under 35 U.S.C §103(a)

Claims 8-18, 33-49, and 51-53 are rejected as obvious over the combination of Rolfes et al., U.S. Pat. No. 6,221,399 ("Rolfes"), in combination with Parikh et al., US patent No. 6,228,399 ("Parikh") and Liversidge. The rejection is traversed to the extent it is applied to the claims as amended.

It is well recognized under U.S. law, that any rejection of a claim for obviousness over a combination of prior art references must establish that: (1) the combination produces the claimed invention; and (2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention.[1] The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention.[2] The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification.[3]

Claims 8, 33, and 43, from which the remaining claims subject to the rejection depend, have been amended to require that the recited hydrophilic inclusion complex consists essentially wherein said hydrophilic complex consists essentially of nano-sized particles of a water-insoluble lipophilic compound surrounded by and entrapped within an amphiphilic polymer. The claims further require that the inclusion complex renders the lipophilic compound soluble in water and bioavailable.

Methods for making inclusion complexes with these features are not taught or suggested by the combination of Rolfes, Parikh, and Liversidge. Rolfes describes a solid interpolymer matrix comprising complexes of two or more complementary polymers (*See*, Rolfes at column 7, lines 1-23). The reference further reports that the two complementary polymers, which are capable of complexing with each other, produce a precipitate or gel (*i.e.*, a physical 3-dimensional network is formed). Rolfes also describes a method using complementary polymers or polymers which form interpolymer matrixes by complexing with each other. However, Rolfes does not teach, and lacks any suggestion of, a method for making inclusion complexes with a single amphiphilic polymer, as the amended claims expressly require.

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[1] *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).
[2] *In re Napier*, 34 U.S.P.Q.2d 1782, 1784 (Fed. Cir. 1995).

Furthermore, Rolfes describes the active agent as becoming incorporated into the interpolymer complex, *e.g.*, embedded or encapsulated in the interpolymer complex (*See*, Rolfes at column 7, lines 26-28 and lines 32-33). Specifically, the incorporation of the active agent into the interpolymer complex creates a viscous environment that encourages a homogeneous distribution of the dispersed drug within the polymer matrix. Rolfes does not teach direct complex formation between the polymer and the active agent, which results from Applicants' claimed methods.

Parikh and Liversidge does not cure the deficiencies of Rolfes. Parikh does not describe a hydrophilic inclusion complex now required by the claims, and also fails to teach or suggest non-interpolymer complexes or inclusion complexes comprising a single amphiphilic polymer, as claimed here. Liversidge, as has been discussed above, lacks any description or suggestion of making particle that is an inclusion complex.

In summary, Applicants submit that the combination of Rolfes, Parikh and Liversidge does not teach or suggest the claimed invention and that one of ordinary skill in the art combining the teachings of Rolfes, Parikh and Liversidge would not produce the present invention. In view of the above, withdrawal of the present rejection is respectfully requested.

In view of the aforementioned remarks and amendments, the Applicants believe that each of pending claims is in condition for allowance. Reconsideration, withdrawal of the rejections, and passage of the case to issue is respectfully requested.

[3] *In re Laskowski*, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

This amendment accompanies a request for continued examination. The Commissioner is authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 23908-501.

Respectfully submitted,

Dated: September 27, 2004

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